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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,045	06/07/2002	Joelle Thonnard	BM45412	6744

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	12

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/088,045	Applicant(s) THONNARD, JOELLE	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,29,32,34,35,38,43,44,46 and 50-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,29,32,34,38,43,44,46 and 50-55* is/are rejected.

7)☒ Claim(s) *35* is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's response to restriction requirement filed on 8/18/03 (Paper # 11) has been entered. Claims 28, 30-31, 33, 36-37, 39-42 and 47-49 have been cancelled. Claims 27, 43, and 44 have been amended. New claims 50-55 have been added. Claims 27, 29, 32, 34, 35, 38, 43-44, 46 and 50-55 are pending in the application.

Information Disclosure Statement

2. Information Disclosure Statement has been filed on 3/14/02 (paper # 3) and a signed copy is attached with this action

Specification - Informalities

3. Claims should begin with "I claim" or "'we claim" or "What is claimed is".

It is noted that Abstract of the Disclosure is missing. If applicant desires to include the abstract from the PCT/EP00/09035 , a copy of the abstract will be inserted in to the specification.

There are no line numbers in the specification pages.

Election

4. Applicant's election Group I, claims 27, 29, 32, 34, 35, 38, 43-44, 46 and 50 –55 (Paper # 11) with respect to SEQID.NO: 2, drawn to polypeptide, fusion polypeptide, immunogenic composition and a method of inducing immune response is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

5. This application 10/088045 is a national stage entry (371) of PCT/EP00/09035, International Filing Date: 01/14/2000, which claims priority to foreign applications UNITED KINGDOM 9921691.3 filed on 09/14/1999 is acknowledged.

The examiner has reviewed Foreign applications, UNITED KINGDOM 9921691.3 filed on 09/14/1999 and find support for the claimed subject matter, an isolated polypeptide, SEQ.ID.NO: 2 (502 amino acids) Accordingly, the subject matter defined in the elected claims, drawn to SEQ ID NO: 2 have an effective filing date of 01/19/2000 that of the PCT/EP00/00428 because an isolated polypeptide comprising an amino acid sequence, SEQ ID NO: 2 (containing 502 amino acids) is first disclosed in this application.

Drawings

6. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See attached PTO-948 for details. Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect may be deferred until after the examiner has considered the proposed drawing correction. Failure to timely submit the proposed drawing correction will result in the abandonment of the application.

Claim Rejections - 35 USC 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying

8. Claims 27, 29, 32, 34, 38, 43-44, 46 and 50 –55 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at

Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

The claims are drawn to an isolated polypeptide comprising SEQ.ID.NO: 2 and an immunogenic fragment comprising at least 15 amino acids or 20 amino acids. Claims are also drawn to fusion protein and immunogenic compostion comprising said fragments, pharmaceutically acceptable carrier and adjuvant.

The specification broadly describes as part of the invention, an isolated protein of SEQ ID NO: 2, which is encoded by BASB 109 gene from M.catarrhalis, strain Mc2931 (ATCC 43617). The specification also teaches on page 65 that this full-length protein contains 502 amino acids. . However, the specification does not teach fragments or immunogenic composition or fusion protein comprising fragments of 15 amino acids or 20 amino acids of SEQ.ID.NO: 2

The actual biological function of the protein represented as SEQ ID NO: 2 is not set forth in this specification. Applicants broadly describe the invention as embracing any deletion by use of language in which a specified percent of amino acids can be changed in the protein. USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, an isolated polypeptide consisting of SEQ ID NO: 2 meets the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth below.

The specification fails to teach an isolated polypeptide fragment of 15 amino acids or 20 amino acids of SEQ.ID.NO: 2 and it is noted that the claimed fragments do not exist as an

invention independent invention. The actual structure or other relevant identifying characteristics of each protein fragment having the claimed properties of the protein can only be determined empirically by actually making it and determine whether such a fragment have the particularly disclosed properties of full length protein. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function. This specification does not teach and is devoid of correlation with full length SEQ ID NO: 2 protein and said protein with an undetermined function. There is no written description support for an isolated fragments comprising 15 amino acids or 20 amino acids or immunogenic composition or fusion protein comprising said fragments as claimed.

The isolated polypeptide comprising SEQ ID NO: 2 is uncharacterized by this specification and is not asserted to belong to any known family of proteins (Outer membrane or transferrin binding protein etc). The specification fails to teach the structure or relevant identifying characteristics of a representative number of SEQ.ID.NO: 2 fragments, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

9. Claims 27, 29, 32, 34, 38, 43-44, 46 and 50-55 are rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide consisting of the amino acid sequence SEQ ID NO: 2, fusion protein comprising the amino acid

sequence SEQ ID NO: 2 and immunogenic composition comprising the amino acid sequence SEQ ID NO: 2 does not reasonably provide enablement for an isolated polypeptide comprising fragments of at least 15 or 20 amino acids of SEQ ID NO: 2, fusion protein and immunogenic composition comprising fragments of at least 15 or 20 amino acids of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches the production of recombinant isolated protein of SEQ ID NO: 2, which is encoded by BASB 109 gene from M.catarrhalis, strain Mc2931 (ATCC 43617), The specification also teaches on page 65 that this full-length protein contains 502 amino acids. The specification discloses the claimed polypeptide can be used as an immunogen and formulating the compositions in Freund's adjuvant to immunize mice for preparing antibodies. However, the specification fails to teach an isolated polypeptide comprising a fragments of at least 15 or 20 amino acids of SEQ ID NO: 2. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid sequences (i.e. fragments) for different aspects of biological activity cannot be predicted a priori and must be determined empirically on a case-by-case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or

asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis in proteins. Such proteins differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Applicants have not taught which residues of SEQ ID NO: 2 can be varied and still achieve a polypeptide that is functional and is capable of use as a diagnostic using immunological means of recognition. The specification has not conceived any other functionally equivalent protein fragments and does not set forth the general tolerance to substitutions and where substitutions could be made to get the claimed fragments. Since, the specification lacks a written description of any fragment of SEQ ID NO: 2, it is not enabled for this language because it fails to enable the skilled artisan to envision the detailed chemical structure of the claimed polypeptide fragments of SEQ ID NO: 2 respectively, as well as how to use the polypeptide fragments, one of skill in the art would be unable to produce these fragments. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

Claim Rejections - 35 USC 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 27, 29, 32, 34, 38, 43-44, 46 and 50-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Helminen et al 1994 (J.Infec.Dis, 170; 867-872).

Claims are directed to an isolated polypeptide comprising (a) an amino acid sequence matching SEQ.ID.NO: 2 and said composition when administered with a carrier induces an antibody response or T-cell response.

Helminen et al 1994 disclose an isolated polypeptide, outer membrane protein i.e., OMP from whole cell lysate in a buffer from M.catarrhalis. The antigen to which an immune response has to be elicited is in general in a hydrophilic phase (i.e., buffer). Mice were immunized with whole cell lysate antigens to mice (page 867, right column through page 868, left column, first paragraph) to produce antibodies. Therefore, it reads on immunogenic composition. It is inherent that the whole cell lysates contain more than one protein and read on fusion proteins as well. Applicant's use of the open-ended term "comprising " in the claim 27 fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Therefore, the claims read on the disclosed isolated polypeptide, OMP from M.catarrhalis. Whole cell lysate from M.catarrhalis appears to contain an isolated polypeptide SEQ.ID.NO: 2. Characteristics such as SEQ.ID.NO: 2 are considered

as inherent properties of the polypeptide that was present in the lysate disclosed by the prior art. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). Since the Office does not have the facilities for examining and comparing applicants' claimed isolated polypeptide comprising SEQ.ID.NO: 2 with the polypeptide of prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

12. Claims 27, 29, 32, 34, 43, 46 and 50, 52-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoehn et al (Infection And Immunity1992, 60; 4695-4703 (1992) and Accession Number Q02219.

Hoehn et al disclose an isolated immunogenic polypeptide comprising 15 or 20 contiguous amino acids of SEQ.ID.NO: 2 (see the attached 100% sequence alignment of Accession Number Q02219 from position 178-211 of SEQ.ID.NO: 2 of the claimed invention with protein of prior art from position 173-206). Neisseria gonorrhoeae expresses several novel outer membrane proteins. One of these, Pan 1, has an apparent molecular mass of 54 kD in electrophoresis and is recognized by serum samples from patients with gonococcal infection (see figures 2 and 3) The presence of antibodies to this protein in patient sera suggests that Pan 1 is expressed during gonococcal infection. Cloned the Pan 1 aniA is reacted with monospecific, polyclonal anti-Pan 1 antiserum indicating that the cloned protein is immunogenic. Thus, the prior art anticipated the claimed invention.

Objection

13. Claim 35 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Status of Claims

14. Claims 27, 29, 32, 34, 38, 43-44, 46 and 50-55 are rejected.

Claim 35 is objected.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

9/24/03

LYNETTE R. F. SMITH
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